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PRE-APPEAL BRIEF REQUEST FOR REVIEW		Docket Number (Optional) 63528(45579)									
	Application Number 10/536,629-Conf. #9252	Filed December 16, 2005									
	First Named Inventor Peter Heegaard et al.										
	Art Unit 1618	Examiner L. H. Schlientz									
<p>Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.</p> <p>This request is being filed with a notice of appeal.</p> <p>The review is requested for the reason(s) stated on the attached sheet(s). Note: No more than five (5) pages may be provided.</p> <p>I am the</p> <table><tbody><tr><td><input type="checkbox"/> applicant /inventor.</td><td>_____ /Andrew W. Shyjan, Ph.D., Esq./ Signature</td></tr><tr><td><input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)</td><td>_____ Andrew W. Shyjan, Ph.D., Esq. Typed or printed name</td></tr><tr><td><input checked="" type="checkbox"/> attorney or agent of record. Registration number _____ 61,294</td><td>_____ (617) 517-5595 Telephone number</td></tr><tr><td><input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____</td><td>_____ April 19, 2011 Date</td></tr></tbody></table> <p>NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.</p> <p><input type="checkbox"/> *Total of <u>1</u> forms are submitted.</p>				<input type="checkbox"/> applicant /inventor.	_____ /Andrew W. Shyjan, Ph.D., Esq./ Signature	<input type="checkbox"/> assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)	_____ Andrew W. Shyjan, Ph.D., Esq. Typed or printed name	<input checked="" type="checkbox"/> attorney or agent of record. Registration number _____ 61,294	_____ (617) 517-5595 Telephone number	<input type="checkbox"/> attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34. _____	_____ April 19, 2011 Date
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Docket No.: 63528(45579)
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Peter Heegaard et al.

Application No.: 10/536,629

Confirmation No.: 9252

Filed: December 16, 2005

Art Unit: 1618

For: DENDRIMER CONJUGATES FOR
SELECTIVE SOLUBILISATION OF PROTEIN
AGGREGATES

Examiner: Schlientz, Leah H.

MS AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

PRE-APPEAL BRIEF REQUEST FOR REVIEW

The following remarks support Applicants' Pre-Appeal Brief Request for Review filed concurrently herewith in the above-referenced application. The remarks are presented in five pages or less filed concurrently with Applicants' Notice of Appeal.

Claims 1-18 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Tomalilia et al. (U.S. 5,714,166) in view of Aldrich Technical Publication, 1997 ("Aldrich").

Applicants respectfully request review of the Final Office Action in the above-referenced application. Applicants are filing the "Pre-Appeal Brief Request for Review" based on the following clear errors and/or omissions in the Final Office Action mailed on October 20, 2010.

Clear Error and/or Omission in the Final Office Action

The Examiner has made a clear error and/or omission at least because the instantly claimed invention is not obvious in view of the cited art. There is simply no motivation to combine the teachings of Tomalia et al. and Aldrich to derive the claimed invention.

Tomalia et al. describe STARBURST(tm) PAMAM dendrimer conjugates, and go on to describe how the choice of the STARBURST(tm) dendrimer components affects the properties of the dendrimers (col. 12, lines 1-18) further exemplified by Fig 2A and 2B with different branch lengths resulting in distinctly different properties.

Additionally, Tomalia et al. describe dendrimer conjugates comprising biological response modifiers, which are bioactive agents which alter the response of the organism to stimuli, such as but not limited to interleukins, interferons, tumor necrosis factor, granulocyte colony stimulating factor, viruses, viral fragments and other genetic materials (col. 19, lines 33-37). Consequently, the concept of biological response modifiers described in Tomalia et al. does not comprise or suggest dendrimer conjugates for selective solubilisation of protein aggregates according to the claimed invention, as the examiner implicitly seems to contend on page 5 of the office action.

Furthermore, Tomalia et al. describe that the dendrimers can have terminal groups, which are sufficiently reactive to undergo addition or substitution reactions (to make conjugates), and examples of such groups for use with the STARBURST(tm) PAMAM dendrimers include amino, hydroxy, mercapto, carboxy, alkenyl, nitrite, allyl, vinyl, amido, halo, urea, oxiranyl, aziridinyl, oxazolinyl, imidazolinyl, sulfonato, silanyl, phosponato, crown ethers, bipyridines, chloromethylphenyl, isocyanato, and isothiocyano (col. 30, lines 17-24).

However, Tomalia et al. does not describe or suggest to modify a DAB dendrimer with terminal urea groups for use as a protein solubilising substance, to which the Examiner also fully agrees. But the Examiner looks to the disclosure of Aldrich to find that unmodified DAB(PA)16 diaminobutane dendrimer is commercially available. From this the Examiner asserts that it would

have been obvious to one of ordinary skill in the art to provide urea as an end group on a known PAMAM dendrimer or a known polypropyleneimine dendrimer, such as the DAB-AM-16 disclosed by Aldrich. Applicants respectfully disagree.

It is the burden of the Office to provide a rationale from the prior art for making the specific claimed modification or combination. The Supreme Court recently addressed nonobviousness of "combination" inventions in *KSR Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007) (KSR). The Court confirmed that it is legally insufficient to merely point to the various recited elements. Instead, the Office must identify the basis for the alleged modification or combination by one of ordinary skill to arrive at the claimed invention.

As is clear from cases such as *Adams*, a patent composed of several elements is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art. Although common sense directs one to look with care at a patent application that claims as innovation the combination of two known devices according to their established functions, it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does. This is so because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known.

Applicants respectfully submit that the Office has failed to meet its burden of providing a rationale for combining the teachings of Tomalia et al. and Aldrich. At the time of the invention neither Tomalia et al. nor Aldrich demonstrated or suggested that there existed a known problem for which the obvious solution would be to modify a DAB dendrimer with a urea terminal group. Indeed, neither Tomalia et al. nor Aldrich provided any other motivation for making the claimed compounds.

Moreover, Tomalia et al. disclose that subtle changes to STARBURST(tm) dendrimers result in distinctly different and unpredictable properties, and that one among many terminal groups which are deemed sufficiently reactive to undergo addition or substitution reactions to make conjugates is urea. The person of skill in the art wanting to solve the problem of providing protein solubilising substances would not be motivated by Tomalia et al. or Tomalia et al. in

combination with the Aldrich Catalogue to arrive at a solution falling within the present claims because neither of these references discusses protein solubilisation.

Furthermore, even if an arbitrary problem could be stated involving the use of urea terminal groups. It is by no means an obvious solution to use the Tomalia et al.'s teaching of STARBURST(tm) dendrimers. One reason being that subtle changes to STARBURST(tm) dendrimers result in distinctly different and unpredictable properties. Given the uncertainty in the combined teachings of Tomalia et al. and Aldrich, a person of skill in the art would not have a reasonable expectation of success of deriving molecules with the claimed properties.

For the reasons discussed, Applicants respectfully request that the foregoing rejections be withdrawn. In view of the above amendment, Applicants believes the pending application is in condition for allowance.

Dated: April 19, 2011

Respectfully submitted,

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